## REMARKS

### *i. Status of the claims*

Claims 21-44 are pending. Claims 23, 25-31, and 34-44 are withdrawn. Accordingly, claims 21, 22, 24, 32, and 33 are under examination. Claims 21, 24, and 33 have been canceled, without prejudice or disclaimer. At the outset, Applicants thank Examiner Haddad for extending to the undersigned the courtesy of a telephone conversation on September 1st to discuss general aspects of this application.

Amendments to claim 22

Purely for the sake of advancing this application toward an allowance, Applicants have amended claim 22 as follows:

Subsection "a)" of claim 22 has been amended to recite "*a polypeptide comprising* ***the*** *amino acid sequence of SEQ ID NO. 6*," instead of "*an*" amino acid sequence.

Subsection "b)" of claim 22 has been amended to (i) delete "*naturally occurring*" and to (ii) recite "*95% sequence identity*" instead of "*90% identical.*" Applicants have also amended this embodiment to qualify such a polypeptide has possessing a functional property. Support for "95%" can be found at page 20, line 28 of the specification.

Subsections "c)" and "d)" of claim 22 have been amended to delete recitation of "*biologically active fragment*" and "*immunogenic fragment*," respectively.

Since claims 21, 24, and 33 have been canceled and claim 22 has been so-amended, Applicants contend that most, if not all, of the underlying grounds for rejecting these claims are now moot. According to Applicants' understanding, therefore, the only remaining issue is enablement of *variants* of SEQ ID NO. 6.

***ii. Contrary to the Examiner's assertion, polypeptide variants that differ by no more than 5% in sequence to SEQ ID NO. 6 are enabled***

The Examiner maintained the rejection of claims 21, 22, 24, 32, and 33 under Section 112, first paragraph. According to the Examiner, the claims are enabled for SEQ ID NO. 6, but not for variants because "the specification does not disclose any representative number of species of the amino acid sequence of SEQ ID NO:6 and, therefore, one skilled in the art cannot identify variants of SEQ ID NO:6." Office Action at page 8, second from last paragraph.

More specifically, the Examiner states that "the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO:6 is essential for maintain[ing] its activity and which changes can be made in the structure of SEQ ID NO: 6 and still maintain[ed] the same function." Office Action at the paragraph bridging pages 2 and 3.

Applicants respectfully disagree with this assessment of the specification and point the Examiner to Table 2 at page 60 of the originally-filed application. There, Applicants disclosed the following residues and domains:

Signature sequences, motifs, and domains:

Ig domains: F46-V117, G153-A221

Signal peptide: M1-G30

Transmembrane domain: T238-T260

potential phosphorylation sites: S110, T106, T296, S37, S99, S227, S281, and Y77

potential glycosylation sites: N104, N192

This information informs the skilled person of what are pertinent portions and characteristics of the polypeptide sequence depicted in SEQ ID NO. 6. Furthermore, a polypeptide that shares "95% sequence identity" with SEQ ID NO. 6 is one that can accommodate no more than 15 different amino acids (SEQ ID NO. 6 contains 310 residues). Moreover, claim 22 requires the claimed variant to be functional. Armed with this

information, therefore, the skilled person would know which residues of SEQ ID NO. 6 could be amenable to modification.

In *In re Wallach* (03-1327), the Board held that a polypeptide sequence alone puts one in possession of all of the entire genus of polynucleotide variants that could possibly encode that polypeptide, and that it is unnecessary to written description support for each and every one of those polynucleotide species.

Applicants contend that, just as there exists degeneracy of the DNA code, there similarly exists amino acid substitutions that can be made to a polypeptide, which are conservative in nature, and which do not alter the basic properties of the residue that is replaced. For instance, a glycine or a serine residue can replace an alanine residue. Applicants disclose at page 11, lines 12-41 what are "conservative amino acid substitutions" that can be made to a polypeptide sequence without disrupting function.

For these reasons, Applicants assert that claim 22 is enabled for any functional polypeptide that is no more than 5% different in sequence to the polypeptide of SEQ ID NO. 6.

***iii. Post-filing date publications corroborate the polypeptide of claim 22 is a junctional adhesion molecule***

Applicants also submit that various post-filing date evidence and literature, which corroborate that the presently claimed polypeptide ("IGFAM-6") is a junctional adhesion molecule 3 homolog. See the enclosed sequence alignment and literature citations that are denoted in the appended "protein report."

***iv. Conclusion***

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 9/9/04

By [signature] #46,785

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5444
Facsimile: (202) 672-5399

for Vid S. Mohan-Ram
Registration No. 55,459

Quick Search: [ ] Name/ID

Incyte

Proteome
BioKnowledge® Library
IPPD ™
*Incyte patented*

# 1870848CB1_DNA_25_PF-0643-USN

**Junctional adhesion molecule 3, JAM2 cell adhesion receptor, binds cells expressing JAM2 or ITGB2, induces leukocyte migration, may participate in inflammatory response**

Gene Symbol/Synonyms 1870848CB1_DNA_25_PF-0643-USN
**Corresponding Human Orthologs** JAM3 INCY:930516.FL1
Mouse: Jam3 [P] [details]
**Gene Families**

Tools

**Gene Ontology**
**Molecular Function** Cell adhesion receptor activity [E]; Protein binding [E,P]; Transmembrane receptor activity [P]... [details]
**Biological Process** Cell adhesion [P]; Cell-cell adhesion [P]; Cell growth and/or maintenance [P]; Cell motility [P]... [details]
**Cellular Component** Plasma membrane [P] [details]

BIOKNOWLEDGE RETRIEVER

**Expression**
**Organ/Tissue** All tissues examined [E]; Most tissues examined [E]; Several tissues [E]; Aorta [E]; Blood [E]; Brain [E]; Colon/large intestine [E]; Heart [E]; Kidney [E]; Placenta [E]... [details]
**Cell Type** Aorta endothelium/endothelial cells [E]; Blood platelets [E]; Myeloid cells [E]; T-lymphocytes [E]; Veins endothelium/endothelial cells [E] [details]
**Tumor Type** not Bladder carcinoma [E] [details]

**Disease**
**Diagnostic Marker**
**Therapeutic Target**
**Molecular Mechanism**
**Negative Correlation**

**Sequence**

**Full** malrrpp...hkssfvi (1..310; 310 aa)
pI: 7.71 MW: 34960 TM: 1 [P]
**Gene** Chromosome: 11q25 Introns:
**3D Structure (PDB)** 1F97_A (37%); 1NBQ_A (34%); 1QZ1_A (27%)... [details]
**Domain** Immunoglobulin domain [details]

PROTEIN SEQUENCE

**Related Proteins**
**H. sapiens** JAM3 (100%); JAM2 (38%); F11R (33%)... [details]
**Patents** 7518734CB1_DNA_18_PF-1535-P (99%)... [details]
**M. musculus** JAM3 (86%); JAM2 (36%); F11R (35%)... [details]
**R. norvegicus** JAM1 (38%); RNU16845 (26%); NCAM1 (27%)... [details]
**D. rerio** NCAM1 (30%); NEO1 (30%); NCAM3 (28%)... [details]
**D. melanogaster** AMA (27%); CG6867 (28%); SNS (23%)... [details]
**C. elegans** WRK-1 (30%); UNC-89 (29%); UNC-5 (28%)... [details]
**S. pombe**
**S. cerevisiae**
**Fungal Pathogens**
**C. albicans**
**Others**

BLAST SUMMARY

**LifeSeq® Foundation** Release 13
**Human Transcripts**

| Transcript ID | | Incyte Gene Description |
|---|---|---|
| INCY:930516 | | |
| INCY:930516.FL5 | [JAM3] | 355-aa form |
| INCY:930516.FL1 | [JAM3] | 310-aa splice form, has additional signal peptide motif |
| INCY:930516.FL6 | | 265-aa splice form, lacks transmembrane motif, has additional signal peptide motif |

**Interactions**
**Protein-Protein Complexes**

**Gene Regulation**
**Induced by**
**Repressed by**
**Not Affected by**

**Protein Modifications**

| GenBank # | PIR # | SWISS-PROT # |
|---|---|---|
| Locus Link # 83700 | Unigene # 419149 | OMIM # 606871 |

*Name*

- JAM3 "junctional adhesion molecule 3"
- FLJ14529 "hypothetical protein FLJ14529"

## *References*

*1151340.* Arrate, M. P., Rodriguez, J. M., Tran, T. M., Brock, T. A., and Cunningham, S. A. Cloning of Human Junctional Adhesion Molecule 3 (JAM3) and Its Identification as the JAM2 Counter-receptor. J Biol Chem 276, 45826-32. (2001).

*1160710.* Liang, T. W., Chiu, H. H., Gurney, A., Sidle, A., Tumas, D. B., Schow, P., Foster, J., Klassen, T., Dennis, K., DeMarco, R. A., Pham, T., Frantz, G., and Fong, S. Vascular endothelial-junctional adhesion molecule (VE-JAM)/JAM 2 interacts with T, NK, and dendritic cells through JAM 3. J Immunol 168, 1618-26. (2002).

*1181603.* Santoso, S., Sachs, U. J., Kroll, H., Linder, M., Ruf, A., Preissner, K. T., and Chavakis, T. The junctional adhesion molecule 3 (JAM-3) on human platelets is a counterreceptor for the leukocyte integrin Mac-1. J Exp Med 196, 679-91. (2002).

*1181652.* Phillips, H. M., Renforth, G. L., Spalluto, C., Hearn, T., Curtis, A. R., Craven, L., Havarani, B., Clement-Jones, M., English, C., Stumper, O., Salmon, T., Hutchinson, S., Jackson, M. S., and Wilson, D. I. Narrowing the critical region within 11q24-qter for hypoplastic left heart and identification of a candidate gene, JAM3, expressed during cardiogenesis. Genomics 79, 475-8. (2002).

*1181669.* Cunningham, S. A., Rodriguez, J. M., Arrate, M. P., Tran, T. M., and Brock, T. A. JAM2 interacts with alpha4beta1. Facilitation by JAM3. J Biol Chem 277, 27589-92. (2002).


**E-mail:** BioKnowledge@incyte.com

**1870848CD1_PRT_6_PF-0643-PCT** 310 aa

**JAM3** 355 aa

Junctional adhesion molecule 3, JAM2 cell adhesion receptor, binds cells expressing JAM2 or ITGB2, induces leukocyte migration, may participate in inflammatory response

Match: Length=310, Identity: 99%, Similarity:99%, Query Overlap: 100%, Subject Overlap: 87%, E-value:0.0, Score:632

```
Query: 1   MALRRPPRLRLCARLPDFFLLLLFRGCLIGAVNLKSSNRTPVVQEFESVELSCIITDSQT 60
           MALRRPPRLRLCARLPDFFLLLLFRGCLIGAVNLKSSNRTPVVQEFESVELSCIITDSQT
Sbjct: 46  MALRRPPRLRLCARLPDFFLLLLFRGCLIGAVNLKSSNRTPVVQEFESVELSCIITDSQT 105

Query: 61  SDPRIEWKKIQDEQTTYVFFDNKIQGDLAGRAEILGKTSLKIWNVTRRDSALYRCEVVAR 120
           SDPRIEWKKIQDEQTTYVFFDNKIQGDLAGRAEILGKTSLKIWNVTRRDSALYRCEVVAR
Sbjct: 106 SDPRIEWKKIQDEQTTYVFFDNKIQGDLAGRAEILGKTSLKIWNVTRRDSALYRCEVVAR 165

Query: 121 NDRKEIDEIVIELTVQVKPVTPVCRVPKAVPVGKMATLHCQESEGHPRPHYSWYRNDVPL 180
           NDRKEIDEIVIELTVQVKPVTPVCRVPKAVPVGKMATLHCQESEGHPRPHYSWYRNDVPL
Sbjct: 166 NDRKEIDEIVIELTVQVKPVTPVCRVPKAVPVGKMATLHCQESEGHPRPHYSWYRNDVPL 225

Query: 181 PTDSRANPRFRNSSSHLNSETGTLVFTAVHKDDSGQYYCIASNDAGSARCEEQEMEVYDL 240
           PTDSRANPRFRNSS HLNSETGTLVFTAVHKDDSGQYYCIASNDAGSARCEEQEMEVYDL
Sbjct: 226 PTDSRANPRFRNSSFHLNSETGTLVFTAVHKDDSGQYYCIASNDAGSARCEEQEMEVYDL 285

Query: 241 NIGGIIGGVLVVLAVLALITLGICCAYRRGYFINNKQDGESYKNPGKPDGVNYIRTDEEG 300
           NIGGIIGGVLVVLAVLALITLGICCAYRRGYFINNKQDGESYKNPGKPDGVNYIRTDEEG
Sbjct: 286 NIGGIIGGVLVVLAVLALITLGICCAYRRGYFINNKQDGESYKNPGKPDGVNYIRTDEEG 345

Query: 301 DFRHKSSFVI 310
           DFRHKSSFVI
Sbjct: 346 DFRHKSSFVI 355
```

Schematic Colors:

| Very Strong | Strong | High | Moderate | Low | Weak |
|---|---|---|---|---|---|
| >95% | 80-95% | 45-80% | 35-45% | 25-35% | 20-25% |